THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellants:	Moodycliffe, et al.
Appl. No.:	10/525,256
Conf. No.:	3290
Filed:	September 13, 2005
Title:	PREVENTING OR TREATING EPITHELIAL TISSUE DAMAGE OR HAIR LOSS
Art Unit:	1635
Examiner:	D. Shin
Docket No.:	112701-818

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANTS' APPEAL BRIEF

Sir:

Appellants submit this Appeal Brief in support of the Notice of Appeal filed on October 27, 2008. This Appeal is taken from the Final Rejection in the Office Action dated May 1, 2008 and the Advisory Action dated October 14, 2008.

I. REAL PARTY IN INTEREST

The real party in interest for the above-identified patent application on Appeal is Nestec, S.A. by virtue of an Assignment dated September 13, 2005 and recorded at reel 016776, frame 0387 in the United States Patent and Trademark Office.

II. RELATED APPEALS AND INTERFERENCES

Appellants' legal representative and the Assignee of the above-identified patent application do not know of any prior or pending appeals, interferences or judicial proceedings which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision with respect to the above-identified Appeal.

III. STATUS OF CLAIMS

Claims 1-3 and 6-8 are pending in the above-identified patent application. Claims 4-5 and 9-32 were previously canceled. Claims 1-3 and 6-8 stand rejected. Therefore, Claims 1-3 and 6-8 are being appealed in this Brief. A copy of the appealed claims is included in the Claims Appendix.

IV. STATUS OF AMENDMENTS

A non-final Office Action was mailed on dated December 26, 2007 in which Claims 1-3 and 6-8 were rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. Appellants filed a Response on March 26, 2008 with amendments to Claims 3 and 7. Appellants amended Claims 3 and 7 to recite, in part, wherein the polynucleotide is a cRNA. A final Office Action was mailed on May 1, 2008 in which the rejection of Claims 1-3 and 6-8 was maintained. Appellants filed a Response to the final Office Action on September 26, 2008. An Advisory Action was mailed on October 14, 2008 in which the Examiner again maintained the rejection of Claims 1-3 and 6-8 for alleged lack of enablement. A copy of the non-final Office Action dated December 26, 2007, the final Office Action dated May 1, 2008 and the Advisory Action dated October 14, 2008 are attached as Exhibits A-C, respectively, in the Evidence Appendix.

V. SUMMARY OF CLAIMED SUBJECT MATTER

A summary of the invention by way of reference to the specification and/or figures for each of the independent claims is provided as follows:

Independent Claim 1 is directed to a composition for preventing or treating epithelial tissue damage (page 3, lines 6-9; page 9, line 14-page 12, line 6) comprising a substance that prevents or treats epithelial tissue damage associated with the expression of glucosylceramide synthase (page 3, lines 6-9; page 9, line 14-page 12, line 6), comprising an RNA polynucleotide antisense to a sequence comprising the glucosylceramide synthase mRNA (page 9, line 14-page 12, line 6).

Independent Claim 6 is directed to a composition for preventing or treating epithelial tissue damage (page 3, lines 6-9; page 9, line 14-page 12, line 6) associated with the expression of glucosylceramide synthase (page 9, line 14-page 12, line 6) comprising, a substance that prevents or treats epithelial tissue damage (page 3, lines 6-9;), comprising an RNA polynucleotide antisense to a sequence comprised by the glucosylceramide synthase mRNA (page 9, line 14-page 12, line 6) in a pharmaceutically acceptable carrier (page 12, lines 25-27).

Although specification citations are given in accordance with C.F.R. 1.192(c), these reference numerals and citations are merely examples of where support may be found in the specification for the terms used in this section of the Brief. There is no intention to suggest in any way that the terms of the claims are limited to the examples in the specification. As demonstrated by the references numerals and citations, the claims are fully supported by the specification as required by law. However, it is improper under the law to read limitations from the specification into the claims. Pointing out specification support for the claim terminology as is done here to comply with rule 1.192(c) does not in any way limit the scope of the claims to those examples from which they find support. Nor does this exercise provide a mechanism for circumventing the law precluding reading limitations into the claims from the specification. In short, the references numerals and specification citations are not to be construed as claim limitations or in any way used to limit the scope of the claims.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Claims 1-3 and 6-8 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirements.

VII. ARGUMENT

A. LEGAL STANDARDS

1. Enablement under 35 U.S.C. § 112, first paragraph

Any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. The standard for determining whether the specification meets the enablement requirement is whether the experimentation needed to practice the invention is undue or unreasonable. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). See also *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) ("The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation."). A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

B. THE CLAIMED INVENTION

Independent Claim 1 is directed to a composition for preventing or treating epithelial tissue damage. The composition includes a substance that prevents or treats epithelial tissue damage associated with the expression of glucosylceramide synthase. The substance includes an RNA polynucleotide antisense to a sequence comprising the glucosylceramide synthase mRNA.

Independent Claim 6 is directed to a composition for preventing or treating epithelial tissue damage associated with the expression of glucosylceramide synthase. The composition includes a substance that prevents or treats epithelial tissue damage. The substance includes an RNA polynucleotide antisense to a sequence comprised by the glucosylceramide synthase mRNA in a pharmaceutically acceptable carrier.

C. CLAIMS 1-3 AND 6-8 SATISFY THE ENABLEMENT REQUIREMENT UNDER 35 U.S.C. §112, FIRST PARAGRAPH

In the Office Action, Claims 1-3 and 6-8 were rejected under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement. Specifically, the Examiner suggests that there is lack of support in the specification for compositions comprising a polynucleotide antisense to glucosylceramide synthase mRNA and compositions that treat or prevent epithelial tissue damage. In support of this contention, the Examiner suggests that there exists no relation between the claimed composition and treating or preventing epithelial tissue damage. In contrast, however, Appellants disagree with the Patent Office's conclusion of lack of enablement and request that the rejections be reconsidered and withdrawn.

An analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. The standard for determining whether the specification meets the enablement requirement is whether the experimentation needed to practice the invention is undue or unreasonable. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991). Appellants respectfully submit that one having ordinary skill in the art would readily be capable of performing the claimed method without undue experimentation.

The claims are directed, in part, toward the use of compositions comprising a polynucleotide antisense to glucosylceramide synthase mRNA and compositions for treating or preventing epithelial tissue damage. The specification sufficiently teaches, and it is well known in the art, that glucosylceramide synthase is associated with epithelial tissue damage, that the regulation of glucosylceramides in maintaining epithelial cell homeostasis is related to

preventing/treating epithelial damage by silencing glucosylceramide synthase expression, and that reducing epithelial cell proliferation is related to preventing/treating epithelial damage. Indeed, the claimed method can be easily practiced without undue experimentation. Accordingly, Appellants respectfully submit that the skilled artisan could make and/or use the invention from the disclosure in the specification without undue experimentation.

The survival and propagation of epidermal cells damaged and/or mutated by stress in the form of UV radiation, pollutants, free radicals, chemical substances and the like leads to epithelial tissue damage. See, specification, page 4, lines 3-4 and page 8, lines 9-18. Whether the damaged cells survive and propagate depends on a balance between proliferation, differentiation and apoptosis of epidermal cells. See, specification, page 7, lines 28-29. This balance is regulated by lipids. See, specification, page 7, line 30. In particular, ceramides inhibit cellular proliferation and induce cellular differentiation and programmed cell death. Conversely, glucosylceramides promote cellular proliferation and prevent cellular differentiation and programmed cell death. See, specification, page 8, lines 4-6. CD_{1d} supports the continued existence of stressed cells by binding glucosylceramide. See, specification, page 8, lines 7-8 and page 10, lines 13-15. Glucosylceramide synthase converts ceramides into glucosylceramides. Therefore, genetic modification or deletion of the glucosylceramide synthase mRNA to reduce the availability of glucosylceramides to CD_{1d} binding blocks the function of CD_{1d} to support the survival and propagation of damaged epidermal cells, thus preventing or treating epithelial tissue damage. That glucosylceramide synthase converts ceramides into glucosylceramides and that CD_{1d} binds to glucosylceramides are well known in the art. Accordingly, Appellants respectfully disagree with the Examiner's statement that "applicant's arguments with regard to the roles of CD1d in phospholipids metabolism that is involved in inflammatory responses have nothing to do with, or support, the claimed composition that is antisense to 'glucosylceramide synthase.'" See, Advisory Action, page 2, lines 9-11.

More specifically, the specification clearly states that CD_{1d} appears to negatively regulate cell apoptosis such that CD_{1d} supports a continued existence of stressed cells (*e.g.*, cells exposed to UV radiation), even when the genetic material of the cell is damaged and/or mutated, which damaged cells will continue to induction of inflammation processes and eventually account for the phenomenon of ageing or, eventually, tumor development. See, specification, page 7, line 26-page 8, line 6. Therefore, in blocking apoptosis and/or modifying endogenous CD_{1d} function,

apoptosis of cells under stress may be promoted, instead of their survival and propagation. See, specification, page 8, lines 14-17.

Further, the Patent Office admits that the glucosylceramide synthase mRNA sequence and antisense technology were both known in the art at the time of the invention. See, Office Action, page 3, lines 16-18. As such, it must follow that the sequence for glucosylceramide synthase was also known to be capable of binding to the glucosylceramide synthase mRNA sequence to prohibit the translation of the glucosylceramide synthase mRNA into glucosylceramide synthase.

Glucosylceramide synthase is generally known in the art to be a pivotal enzyme in the biosynthesis of, and catalyses the transfer of, glucose from UDP-glucose (UDP-Glc) to ceramide to form glucosylceramide (GlcCer), the common precursor of most higher-order glycosphingolipids. Therefore, glucosylceramide synthase is critical to the production of GlcCer.

GlcCer is known to be capable of blocking and/or modifying biological CD_{1d} function (*e.g.*, GlcCer is capable of blocking the CD_{1d} receptors from binding with natural killer T-cells and, thus, reduces or prevents inflammatory and/or immunosuppressive reactions). See, specification, page 11, lines 5-26. The specification clearly states that "ceramides are associated with inhibition of cellular proliferation, induction of cellular differentiation and programmed cell death. In contrast, GlcCer induce cell proliferation and inhibit programmed cell death." See, specification, page 7, line 26-page 8, line 6. Thus, since GlcCer is able to block and/or modify biological CD_{1d} function, GlcCer is capable of promoting apoptosis, which is desirable in instances where cells have experienced damage but are capable of proliferating to potentially cause ageing and/or tumor development. It would be beneficial, instead, for such stressed cells to be terminated to reduce or eliminate the risk of aging and/or tumor development.

Therefore, based on the above information, it must follow that an RNA polynucleotide antisense to a sequence comprising the glucosylceramide synthase mRNA is capable of binding to the glucosylceramide synthase mRNA to prohibit the formation of glucosylceramide synthase, which will, in turn, reduce or eliminate the production of glucosylceramide. The reduction or elimination of glucosylceramide will, in turn, reduce damaged cell proliferation thereby preventing or treating epithelial tissue damage as is required, in part, by the present claims. For at least these reasons, Appellants respectfully submit that it is only with a misunderstanding of

the present claims, specification and/or state of the art at the time of filing of the present application that the Examiner is able to maintain the present enablement rejection.

Moreover, Appellants reiterate that the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the specification coupled with information known in the art without undue or unreasonable experimentation. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991). Further, compliance with the enablement requirement of 35 U.S.C. §112, first paragraph, does not turn on whether an example is disclosed. See MPEP 2164.02. An example may be "working" or "prophetic." A working example is based on work actually performed. A prophetic example describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved. *Id.* Accordingly, Appellants need not have actually reduced the invention to practice prior to filing and the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 (CCPA 1970). Nevertheless, Appellants have provided examples in the specification supporting the practice of the present claims.

While the application may not disclose working examples of tests performed using the presently claimed substances and methods with humans, Appellants respectfully submit that this is not dispositive. For example, it is generally accepted in the art that mice are proven experimental models for determinations as to possible effects of new drugs and compounds for use in humans. In this case, the teachings and examples disclosed in Appellants' specification teach the skilled artisan how to make and use the claimed invention for treatment of mice using the presently claimed substances. Indeed, the examples found at pages 54-75 support a role for CD_{1d} in the regulation of phospholipid metabolism which controls inflammatory processes. The examples also demonstrate that blocking CD_{1d} upregulates genes trolling hair follicle development, and down-regulates genes involved in inflammation and cancer development. Consequently, one having ordinary skill in the art can reasonably conclude that by administering the compositions of the present claims to human subjects, CD_{1d} may act to down-regulate genes involved in inflammation and cancer development in accordance with the present claims. In fact, the specification even states that it has been surprisingly found that CD_{1d} gene transcription in

mouse skin is responsive to external stress, such as UV radiation, which finding has been confirmed in human keratinocytes. See, specification, page 7, lines 21-23 (emphasis added).

Although CD_{1d} is not the claimed target gene, as noted by the Examiner in the Advisory Action at page 2, line 11, CD_{1d} is one of the receptors via which the previously mentioned lipids fulfill their biological task. Specifically, CD_{1d} seems to negatively regulate apoptosis such that CD_{1d} supports a continued existence of stressed cells (*e.g.*, cells exposed to UV radiation), even when the genetic material of the cell is damaged and/or mutated, which damaged cells will continue to induction of inflammation processes and eventually account for the phenomenon of ageing or, eventually, tumor development. See, specification, page 7, line 26-page 8, line 6. Therefore, in blocking apoptosis and/or modifying endogenous CD_{1d} function by eliminating or reducing the availability of glucosylceramides to CD_{1d} binding, apoptosis of cells under stress may be promoted, instead of their survival and propagation. See, specification, page 8, lines 14-17. Accordingly, while the target gene may not be CD_{1d}, the presently claimed compositions are effective in blocking apoptosis and/or modifying endogenous CD_{1d} function.

Similarly, the activity of regulatory molecules that control epithelial homeostasis such as ceramides and/or glucosylceramides, may be modified such that they also exert the desired effect on the CD_{1d} molecule. To this end, the number of the glucosylceramide synthase transcripts may be reduced by designing a polynucleotide antisense to at least a part of the glucosylceramide synthase gene or glucosylceramide synthase mRNA, so that eventually the signal to epithelial cells to proliferate is turned down. See, specification, page 10, lines 13-24.

Therefore, based on at least the information set forth above, which contains information that was known in the art and information that is disclosed in the specification, Appellants respectfully submit that the skilled artisan would be able to practice the present invention without undue experimentation.

Accordingly, Appellants respectfully submit that Claims 1-3 and 6-8 fully comply with 35 U.S.C. §112, first paragraph, and are in condition for allowance.

VIII. CONCLUSION

Appellants respectfully submit that Claims 1-3 and 6-8 meet the requirements of 35 U.S.C. §112, first paragraph. Accordingly, Appellants respectfully submit that the enablement rejection is erroneous in law and in fact and should therefore be reversed by this Board.

Respectfully submitted,

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Dated: December 3, 2008

CLAIMS APPENDIX

PENDING CLAIMS ON APPEAL OF U.S. PATENT APPLICATION SERIAL NO. 10/525,256

1. A composition for preventing or treating epithelial tissue damage comprising a substance that prevents or treats epithelial tissue damage associated with the expression of glucosylceramide synthase, comprising:

an RNA polynucleotide antisense to a sequence comprising the glucosylceramide synthase mRNA.

2. The substance according to claim 1, further comprising a cell containing the polynucleotide and a lower amount of the CD_{1d} gene translation product than in similar cells lacking the polynucleotide.

3. The substance according to claim 1, wherein the polynucleotide is a cRNA.

6. A composition for preventing or treating epithelial tissue damage associated with the expression of glucosylceramide synthase comprising, a substance that prevents or treats epithelial tissue damage, comprising:

an RNA polynucleotide antisense to a sequence comprised by the glucosylceramide synthase mRNA in a pharmaceutically acceptable carrier.

7. The composition according to claim 6, wherein the polynucleotide is a cRNA.

8. The composition of claim 6, further comprising a cell containing the polynucleotide and a lower amount of the CD_{1d} gene translation product than in similar cells lacking the polynucleotide.

EVIDENCE APPENDIX

EXHIBIT A: Non-Final Office Action dated December 26, 2008

EXHIBIT B: Final Office Action dated May 1, 2008 ("Office Action")

EXHIBIT C: Advisory Action dated October 14, 2008

RELATED PROCEEDINGS APPENDIX

None.